

Relation of Serum Magnesium Level in Adult Patients with Idiopathic Generalized Epilepsy in a Tertiary Care Hospital

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Magnesium plays a vast role in the nervous system. In particular, high magnesium in cerebrospinal fluid appears to enhance the neural functions, while low magnesium induces neuronal diseases. The aim of the study was to find out the relation of serum magnesium with idiopathic generalized epilepsy attending in a tertiary care hospital. This cross-sectional comparative study was conducted in the department of Neurology at Mymensingh Medical College and Hospital, Bangladesh from January 2019 to June 2020 following ethical approval. Total 110 purposively selected participants (55 with idiopathic generalized epilepsy and 55 non epileptic apparently healthy individuals) were enrolled in this study. Serum total Mg was measured by EMP-168 Biochemical Analyzer. Average age of epileptic individuals was 33.13±9.5 years and majority was female (60.0%). Mean serum magnesium level was lower in epileptic patients than controls (1.80±0.041 vs. 2.02±0.19 mg/dl; p<0.001). Patients with higher seizure attack (>3 per month) had significantly lower mean serum magnesium level than the patients with seizure attack three or less per month. Serum magnesium levels are reduced in epileptic patients compared to healthy age and gender matched controls. Studies involving larger numbers of patients are needed to confirm these results.

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Key words: Serum magnesium level, Epilepsy, Idiopathic generalized epilepsy

Introduction

Epilepsy is one of the most common neurological diseases and affects people of all ages, races, social classes and geographical locations¹. About 50 million people around the world have epilepsy, as reported by the World Health organization². Regarding the prevalence of epilepsy in Bangladesh, no national statistics is available, but it has been estimated that at least 1.5-2.0 million people are suffering from epilepsy in our country, i.e. about 10-12 per 1000 people and common age group is from 16-31 years mostly^{3,4}. As epilepsy affects both economy and quality of life, proper management of the disease may improve the prognosis of the patients and reduces the burden of cost of both family and the government. In this regard there is a need to consider different influences on ictogenesis and its modification in order to reduce seizures in the people with epilepsy. Dietary and lifestyle factors may also have an influence on seizures, and magnesium (Mg) is one of such potential factor contributing seizures. The fourth most prevalent mineral in the body, Mg is essential in more than 300 enzyme systems, including all adenosine triphosphate enzymes^{5,6}. It is mainly found in the muscles, erythrocyte, soft tissues and bone. Because the excess amount of Mg is excreted via

kidneys, constant intake of Mg is necessary⁷. The inhibitory role of Mg in the CNS has been confirmed⁸.

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According to literature, Mg inhibits the stimulatory effect of calcium and N-methyl-D-aspartate (NMDA). Mg reduces the release of acetylcholine in the site of the neuromuscular junction, so it leads to reduction of excitatory activity of nerve fibers and decreases the risk of seizure. It has been documented that seizure is firmly related to glutamatergic neurotransmission. Extracellular Mg reduces spontaneous spikes in the seizure via the NMDA receptor and hyper excitability of the neuronal surface. It is well documented that severe Mg deficiency can lead to seizure activity^{9,10}. Recent studies have also shown that people with epilepsy have lower Mg levels than people without epilepsy^{11,12,13,14}. To the best of our knowledge, no such study has been yet conducted in Bangladesh, indicating that the Mg level of epileptic patients and its association with idiopathic seizure was not studied much. Because epilepsy is a common problem in our country, this study was designed to investigate the status of serum Mg in patients with idiopathic generalized epilepsy and compared it with apparently healthy individuals without history of epilepsy.

Methods

This cross-sectional comparative study was conducted in the Department of Neurology of Mymensingh Medical College Hospital, Mymensingh, Bangladesh over one and half year from January 2019 to June 2020. Informed written consent was obtained from the participants before enrollment. The study protocol was approved by the Ethical Review Committee of Mymensingh Medical College (Memo No.: MMC/IRB/2019/113 Date: December 28, 2020). A total of 55 diagnosed case of idiopathic generalized epilepsy aged more than 18 years who experiences one or a combination of generalized seizure type like tonic clonic, myoclonic, absence were included in the study. Patients with gastrointestinal disorders such as chronic diarrhea and malabsorption syndromes, on diuretics such as frusemide, thiazides and acetazolamide, epileptic patients with known structural brain diseases and secondary causes of epilepsy, alcoholics, patients with chronic renal disease, pregnant women and critically ill patients requiring ICU support were excluded. Equal number of apparently healthy controls without epilepsy matched to cases by age and gender were

included as a comparison group. The data collected included socio-demographic profile (age and sex, residential location, monthly family income) and epilepsy characteristics (family history of epilepsy, duration of epilepsy and frequency of seizure). Three ml of blood samples were collected by venipuncture into EDTA containing tubes and immediately sent to emergency biochemistry lab of Department of Cardiology, Mymensingh Medical College Hospital. Within automated analyzer machine, automatically 200 μ l of sample serum from each tube was drawn and mixed with reagents. Serum magnesium was measured using EMP-168 Biochemical Analyzer (Brussels, Belgium) using the modified Trinder technique. The test was done at room temperature. Within 3 min, result was shown in computer display & print was taken by clicking print. Then the reading was noted in mg/dl. Lab reference value was 1.80-2.20mg/dl. Data were analyzed by using SPSS version 23.0. Qualitative variables were summarized by percentage. Quantitative variables were summarized by mean and standard deviation (SD) or median and interquartile range. The independent sample t-test or one way analysis of variance (ANOVA) or F test was used to assess the difference of mean serum magnesium level among groups. A 2-tailed $p < 0.05$ was considered to be statistically significant in all analyses.

Results

In the current study mean age of the patients with idiopathic generalized epilepsy was 33.13 ± 9.5 years and majority of the patients were in 21-40 years age group. Majority of the patients were female (60.0%) with a female to male ratio of 1.5:1. Family history of epilepsy was in 21.8% of the patients. In majority of the patients (21.8%) duration of epilepsy was less than one year and 63.63% reported a monthly seizure frequency of three or less (Table I).

Table II showed that mean serum magnesium level was 1.80 ± 0.04 mg/dl in epileptic patient's group and 2.02 ± 0.19 mg/dl was in non-epileptic group. This difference was highly significant statistically ($p < 0.01$).

Serum magnesium level of epileptic patients did not significantly varies with age ($p = 0.62$) (Table III).

Table I: Characteristics of the patients with idiopathic generalized epilepsy (n=55)

Variables	Frequency (n)	Percentage (%)
Age in years (Mean±SD)		33.13±9.5
<i>Sex</i>		
Female	33	60.0
Male	22	40.0
<i>Residence</i>		
Urban	16	29.1
Rural	39	70.9
Monthly family income, median (IQR), BDT	18,000 (14,000-23,000)	
<i>Family history of epilepsy</i>		
Present	12	21.8
Absent	43	78.0
<i>Duration of epilepsy (years)</i>		
<1	33	60.0
1-3	09	16.4
>3	13	23.6
<i>Seizure frequency per month</i>		
≤3	35	63.63
>3	20	36.36
<i>EEG Findings</i>		
Positive	21	38.18
Normal	34	61.81

IQR: Interquartile range; BDT: Bangladeshi taka

Table II: Serum magnesium in idiopathic seizure cases and healthy controls

Study group	Serum magnesium level (mg/dl)		p value (Independent samples t-test)
	Mean±SD	Range	
Idiopathic seizure cases (n=55)	1.80±0.04	1.76-2.01	0.001
Healthy controls (n=55)	2.02±0.19	1.81-2.50	

Table III: Relation between age and serum magnesium level patients with idiopathic generalized epilepsy (n=55)

Age groups (years)	Serum magnesium (mg/dl)	p value (One-way ANOVA Test)
	Mean±SD	
≤20	1.81±0.07	0.62
21-30	1.79±0.03	
31-40	1.79±0.02	
41-50	1.79±0.01	
≥50	1.80±0.03	

Table IV shows that mean serum magnesium level of male or female epileptic patients were similar ($p=0.22$).

Table IV: Comparison of serum magnesium level between male and female patients with idiopathic generalized epilepsy (n=55)

Sex	Serum magnesium (mg/dl)	p value (Independent samples t test)
	Mean±SD	
Male (n=22)	1.79±0.02	0.22
Female (n=33)	1.80±0.05	

Table V demonstrated the relation between frequency of epileptic attacks and serum magnesium level. It depicted that, mean serum magnesium level was significantly lower in patients with more than three seizure attack than the patients had monthly seizure attack three or less. However, serum magnesium level had no relation with the duration of epilepsy.

Table V: Relation of serum magnesium with duration of epilepsy and frequency of seizure in patients with idiopathic generalized epilepsy (n=55)

Variables	Serum magnesium level (mg/dl)	p value
	Mean±SD	
<i>Duration of epilepsy (year)</i>		
<1	1.79±0.10	0.571 [†]
1-3	1.79±0.042	
>3	1.78±0.20	
<i>Seizure frequency per month</i>		
≤3	1.79±0.02	0.020*
>3	1.77±0.03	

[†]One- way ANOVA (F test); *Independent samples t test.

Discussion

For a lot of various actions within human body, Magnesium is well known. In the nervous system magnesium is essential for healthy nerve by taking role in neuronal transmission and neuromuscular conduction. It also have protective role against excessive excitation (excitotoxicity) that leads for its diverse actions within the human body. From a neurological standpoint, magnesium plays an essential role in nerve transmission and neuromuscular conduction. It also functions in a protective role against excessive excitation that can lead to neuronal cell death (excitotoxicity) and has been implicated in multiple neurological disorders. Due to these important functions within the nervous system, magnesium is a mineral of intense interest for the potential prevention and treatment of neurological disorders⁸. The present study was conducted in the Department of

Neurology, Mymensingh Medical College Hospital to determine the role of serum magnesium level in idiopathic generalized seizure, which was compared to apparently healthy controls without epilepsy. In this current study mean age of epileptic patients was 33.13±9.5 years and majority of the respondents were between 21-40 years of age. Female were more than male with a female to male ratio of 1.5:1. Age and sex distribution of the patients with epilepsy of the present study was comparable to the other local and international studies^{4,11,12,13,14,15}. Present study demonstrated that patients with idiopathic generalized epilepsy had significantly lower magnesium compared with those of healthy controls, even though both values were within the reference interval. Although there are no available local studies, few studies conducted in other countries were in agreement with the present study

findings^{11,12,15,16}. Oladipo et al.¹¹ observed the mean plasma magnesium in the patients was 0.98 mmol/L while that in the controls was 1.15 mmol/L. In the study of Sinert et al.¹² among 49 patients with seizure and 32 healthy racially matched controls, patients had a significantly lower mean ionized magnesium level. Abdullahi et al.¹⁵ observed that the mean serum magnesium level was significantly lower among people with epilepsy compared with the controls (0.79±0.18 mmol/L vs. 0.90±0.17 mmol/L, $p = 0.007$). Lee et al.¹⁶ reported that serum magnesium levels decreased significantly in patients with seizure disorders when compared to controls. Duration of epilepsy was not associated with a significant difference in serum magnesium concentrations. However, a relationship between fall in mean magnesium level and higher seizure frequency was noted in the present study. These findings were consistent with a previous study which also found that serum magnesium levels are negatively correlated with epilepsy frequency¹⁷. The evidence that low levels of magnesium can cause seizure-like discharges had been observed in experimental slices of human epileptogenic neocortex obtained during neurosurgical procedures. According to this study and previous study suggests that low serum magnesium may play a role in epilepsy. So, the correction of magnesium deficiency may result in better seizure control for some patients.

Conclusion

In conclusion, this study demonstrated that serum magnesium level is lower in the idiopathic generalized epilepsy patients in comparison to healthy control group. Significantly lower serum magnesium is also noted in epileptic patients having increased frequency of seizure per month.

Limitations

Due to cross-sectional design of the study it was not possible to make comment about the causation. Small sample size, purposive sampling technique and sample from a single government level tertiary care hospital were some of the other limitations of the present study. We measured the total free magnesium rather than ionized magnesium level which would have given a better level of physiologically active form that is in equilibrium with the intracellular magnesium. Finally, confounding variables were not

eliminated and apparently healthy respondents were chosen from the same source of cases.

Recommendations

All patients with epilepsy could be screened for serum magnesium. Nevertheless, given limitations of the present study, it seems that there is a need for further researches with larger sample sizes or different methodologies to show the role of Mg in epileptic seizure.

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